PATENT
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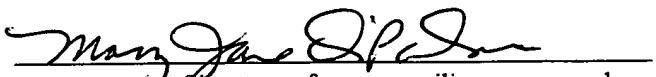
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Jeffrey A. Hubbell *et al.*	Art Unit:	1615
Serial No.:	09/118,242	Examiner:	Todd Ware
Filed:	July 17, 1998		
Title:	BIODEGRADABLE MACROMERS FOR THE CONTROLLED RELEASE OF BIOLOGICALLY ACTIVE SUBSTANCES		

Assistant Commissioner of Patents
Washington, D.C. 20231

DECLARATION OF DR. JEFFREY HUBBELL UNDER 37 CFR §1.132 TRAVERSING GROUNDS OF REJECTION

Under 37 CFR §1.132 and regarding the rejection of claims 1-26, 30-31, and 40-43 on reference to U.S. Patent No.: 5,410,016, I declare:

1. I am an inventor of the subject matter described and claimed in the above-captioned patent application.

2. I have read the Office Action mailed April 13, 1999.

3. The present invention features methods for making and delivering biologically active substances. The biologically active substances are contained in macromers, and comprise at least 5% active substance by weight. I believe that one skilled in the art of sustained release drug delivery would not have been motivated to make macromers containing such a high percentage of biologically active substance. Historically, it has not been deemed desirable to load macromers with the large amounts of biologically active substance as claimed in the present invention, due to the inherent tendency of these compositions to release additional biologically active substance very early in the delivery time frame. At the time the present application was filed, the field of polymers was such that one skilled in the art would not be motivated to use known polymers or to how to design macromers, as described in the present invention, that contain 5%, or more, biologically active substance, by weight. The reason why one skilled in the art would not be motivated to use polymers containing at least 5% biologically active substance by weight involves the amount of "burst" (the early peak release of drug) associated with such high loading, as addressed below.

4. At the time of filing the present application the state of the art was such that it was believed that increased bursting occurred as the macromers were loaded with

increasing amounts of biologically active substance. This viewpoint is supported by examples cited in Hubbell '016, wherein a macromer was loaded with 3.3% lysozyme by weight, and 25% of the lysozyme was released at 24 hours after exposure to PBS, and 75% of the lysozyme was released at 48 hours (see Hubbell art figure 3b). Such a large burst is a highly undesirable feature in sustained release composition as the goal of such compositions is to deliver a steady even amount of drug over the appropriate time period. In another example, involving BSA loaded macromers, the BSA was released from the macromer with no bursting. However, the amount of BSA loaded into the macromer was only 0.1%, (see Hubbell art figure 3a) an amount which is too low to be therapeutically useful. For reasons based on the above examples of burst in sustained release drug delivery polymers loaded with less than 5% biologically active substance by weight, and the comments provided herein, the present invention is not obvious, because one skilled in the art of sustained drug release delivery polymers would have believed that high loading of such polymers would only exacerbate the problem of burst.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may

jeopardize the val [illegible]ity of the application or any patents issued thereon.

17. April 2000
Date

Jeffrey A. Hubbell, Ph.D

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